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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,647	11/27/2001	Bernd Riedl	BAYER 18A	1010

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/993,647	RIEDL ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74,81,87,93 and 99-116* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74,81,87,93 and 99-116* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040507& 20040512*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on September 13, 2005 has been entered.

Claims 74, 81, 87, 93 and 99-116 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 74, 81, 87, 93 and 99-116 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the *in vitro* treatment of the tumor cell lines HCT116 and DLD-1, does not reasonably provide enablement for a method for the treatment of all types of solid tumors, carcinomas, myeloid disorders or adenomas. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The

nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to 'a method for the treatment of solid tumor' or 'a method for the treatment of a carcinoma, myeloid disorder or adenoma' and according to the specification, the compounds are useful in the treatment of solid cancers such as carcinomas, myeloid disorders or adenomas, see specification page 2, lines 5-17. First, the instant claims cover 'solid tumors', 'carcinomas', 'myeloid disorders', and 'adenomas' that are known to exist and those that may be discovered in the future, for which there is no enablement provided.

Note: Solid tumor is a cancer of body of tissues other than blood, bone marrow or the lymphatic system. Carcinoma is any cancer that arises from epithelial cells. Myeloid leukemia is a malignancy of immature bone marrow cells. Adenoma is a collection of growths of glandular origin.

No compound has ever been found to treat solid tumors, carcinomas, myeloid disorders or adenomas of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004).

Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against solid tumors, carcinomas, myeloid disorders or adenomas in general.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating several types of solid cancers, carcinomas, myeloid disorders, and adenomas.

2) The state of the prior art: There are no known compounds of similar structure, which have been demonstrated to treat all types of the cancers recited in the claims. Stein (document enclosed) provides that "the physician's approach to the treatment of patients with cancer varies depending on the following features: organ of origin, histology and stage, paraneoplastic syndromes, age of the patient and presence of other morbid diseases" (see page 707). Further, the reference provides that "Cancer represents hundreds of diseases with many causes. Although each disease may share certain general features with others, the approach to therapy for a give problem will vary" (see page 708).

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to protect a potential host from the disorders embraced by the instant claims nor there are doses given for the treatment of the disorders recited. The specification provides assays (see pages 94-96) to test the compounds *in vitro* and discloses that the compounds exhibit RAF kinase inhibitory properties. However, there is no demonstrated correlation that the tests and results apply to all of the disorders embraced by the instant claims.

6) The breadth of the claims: The instant claims embrace the treatment of all types of solid tumors, carcinomas, myeloid disorders and adenomas. See *In re Vaeck*, 947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above. The state of the art provides that "Adult acute myeloid leukemia (AML) and the myelodysplastic syndromes (MDS) remain a formidable therapeutic challenge" (see Crump, Medline Abstract).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 74, 81, 87, 93 and 99-116 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 67, 73, 78, and

83 of copending Application No. 10/042,226. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed methods of use of the compounds are substantially embraced by the reference claims. The reference claims are also drawn to a method for the treatment of cancers including carcinomas, myeloid disorders, adenomas, using phenyl urea compounds, which include the compounds recited in the instant claims. One of ordinary skill in the art would have been motivated to select the compounds of the instant claims from the list of compounds recited in reference claims because such compounds would have been suggested by the reference as a whole because the skilled artisan would have had reasonable expectation that any of the compounds would have had the same use taught for the genus as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

2. Claims 74, 81, 87, 93 and 99-116 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 67 of copending Application No. 09/948,915. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed methods of use of the compounds are substantially embraced by the reference claims. The reference claim is also drawn to a method for the treatment of cancerous cell growth using phenyl urea compounds, which according to the reference disclosure includes treatment of solid tumors, carcinomas, myeloid disorders, adenomas. The reference claimed method recites a list of compounds that are used in the method, which includes the use of compounds recited in the instant claims. One of

ordinary skill in the art would have been motivated to select the compounds of the instant claims from the list of compounds recited in reference claims because such compounds would have been suggested by the reference as a whole because the skilled artisan would have had reasonable expectation that any of the compounds would have had the same use taught for the genus as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Claims 74, 81, 87, 93 and 99-116 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 36 and 40 of copending Application No. 10/361,850. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly claimed methods of use of the compounds are substantially embraced by the reference claims. The reference claims are also drawn to a method for the treatment of raf-mediated disorders, which include tumor growth, etc. using a generic group phenyl urea compounds. The reference genus includes the compounds recited in the instant claims. One of ordinary skill in the art would have been motivated to select the compounds of the instant claims from generic group of compounds recited in reference claims because such compounds would have been suggested by the reference as a whole because the skilled artisan would have had reasonable expectation that any of the compounds would have had the same use taught for the genus as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Information Disclosure Statement

Receipt is acknowledged of the Information Disclosure Statement filed on May 7, 2004 and May 12, 2004 and copies are enclosed herewith. Applicant's attention is directed to the IDS filed on May 7, 2004 wherein each of the sheets were identified as "Sheet 1 or 18"; "Sheet 5 of 18"; "Sheet 9 of 18"; "Sheet 17 of 18"; and "Sheet 18 of 18", however, there were only five (5) PTO-1449 sheets found, which are renumbered as sheets 1 through 5 of 5.

Conclusion

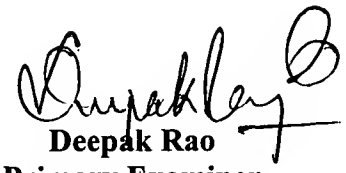
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Deepak Rao
Primary Examiner
Art Unit 1624

June 23, 2006